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Synthesis and Herbicidal Activity of Substituted Tetrahydronaphthalenes (Part II)

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Abstract: This paper reports the synthesis and the biological activity of novel tetrahydronaphthalenes with substitution of functional groups at each position of the aromatic ring and substitution of various alkyl groups at the 1-position of the non-aromatic ring. These compounds exhibited pre-emergent herbicidal activity which was determined by the orientation and type of functional groups on the aromatic ring with the 1,1-dimethyl substitution on the non-aromatic ring. The activity tended to be highest for nitro or methyl at the 5- and 7-positions with an amino or ester group at the 6-position and a dimethyl substitution at the 1-position.

Key words: tetrahydronaphthalene, tetralin

1 INTRODUCTION

As part of our tetrahydronaphthalene studies,[1,2] we investigated what effect the functional group substitution on the various positions of the aromatic ring had on herbicidal activity. In Part I of the series, the effects of substitution at the 5- and/or 7-position of 6-alkyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalenes (tetralins) were reported.[3] These results prompted further exploration of what effect the substitution of functional groups at all positions of the aromatic ring with various alkyl groups at the 1-position of the non-aromatic ring would have on the herbicidal activity.

The herbicidal activity of these compounds has been optimized by varying the orientation and nature of the substituents on the aromatic ring (R_5–R_8) while maintaining a dimethyl substitution at the 1-position (R_1, R'_1) on the non-aromatic ring of the general structure of the tetrahydronaphthalene or tetralin (Fig. 1).

2 EXPERIMENTAL

2.1 General

The compounds prepared, together with their physical properties, are shown in Tables 1–9. Nuclear magnetic resonance spectra (^1H, ^{13}C, ^{19}F) were recorded using either a Bruker WM-360 or a Varian XL-400 NMR spectrometer. Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, GA. Sample purity was determined by gas liquid chromatography (GLC) analysis on a Varian 3400 gas chromatograph utilizing a 1/8″ ID × 6′ (3.2 mm × 1.83 m) stainless steel column packed with 10% Supelco SP-2100 (methyl silicone) on 80/100 Supelcoport. Normally, a temperature program from 150°C to 300°C at 15°C min^{-1} was employed. Column chromatography was performed on a Waters preparative liquid chromatography (LC) Model 500 using silica gel columns. Most reported yields are unoptimized.

2.2 Synthesis

A generalized synthesis is shown in Fig. 2. The alcohols were cyclodehydrated using polyphosphoric acid (PPA) to afford the tetralin intermediates. These intermediates were nitrated to yield both the mono- and dinitrotetralins and were further derivatized by nucleophilic displacement of a fluorine. The tetralin intermediates could also undergo a Friedel–Crafts acylation to yield the acyltetralin which was then oxidized using the haloform reaction to afford the free acid, and from the latter carboxylate esters and amides were prepared. Specific

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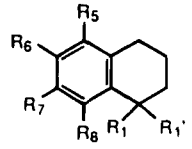


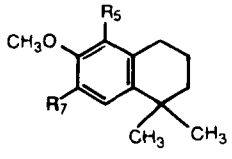
Fig. 1. General structure of substituted tetrahydronaphthalenes.

detailed reaction schemes for the syntheses and derivatization of each of the tetralins are described within Refs 1 and 2.

The synthesis of the tetralin derivatives has been accomplished following the procedures described below.

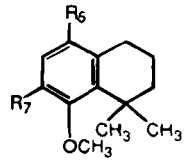
2.2.1 Procedure A: general procedure for cyclodehydration of alcohols (**1a**, **2a**, **5a–d**, **7a–e**)
The alcohol (0·010 mol) was added dropwise to a slightly cooled solution of polyphosphoric acid (PPA) (10·0 g) using a mechanical stirrer. The solution was monitored during addition to maintain a temperature between 15 and 25°C. Upon complete addition, the solution was stirred at room temperature for 4 h, poured over ice/water (200 g) and subsequently extracted with diethyl ether. The ether layer was washed with water and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the product. The product was purified

TABLE 1
Tetralins of Structure **1**



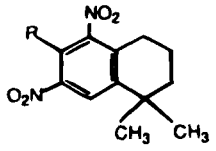
Entry	R_5	R_7	*Yield* (%)	*m.p.* (°C)
1a	H	H	86	–
1b	NO_2	H	50	–
1c	H	NO_2	50	130–131
1d	NO_2	NO_2	64	109–110
1e	H	$COCH_3$	89	79 80
1f	H	CO_2H	100	132 133
1g	H	CO_2CH_3	90	114–115

TABLE 2
Tetralins of Structure **2**



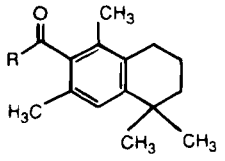
Entry	R_5	R_7	*Yield* (%)	*m.p.* (°C)
2a	H	H	14	
2b	NO_2	NO_2	64	87–88
2c	$COCH_3$	H	82	–
2d	CO_2H	H	99	192–193
2e	CO_2CH_3	H	72	

TABLE 3
Tetralins of Structure **3**



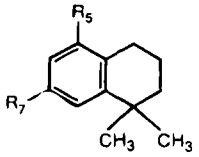
Entry	*R*	*Yield* (%)	*m.p.* (°C)
3a	$NHCH_3$	76	108–109
3b	$N(CH_3)_2$	85	149–150
3c	NHC_2H_5	91	87–88
3d	$N(C_2H_5)_2$	73	86 87
3e	$N(C_3H_7)_2$	61	105–106
3f	$NHCH(C_2H_5)_2$	86	–
3g	SC_2H_5	90	97–98
3h	$SO_2C_2H_5$	76	152–153

TABLE 4
Tetralins of Structure **4**



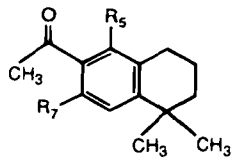
Entry	*R*	*Yield* (%)	*m.p.* (°C)
4a	CH_3	79	102–103
4b	C_2H_5	87	–
4c	CBr_3	89	113–114
4d	OH	56	211–213
4e	OCH_3	76	–
4f	OC_2H_5	93	–
4g	OC_4H_9	75	
4h	$N(CH_3)_2$	71	97 98

TABLE 5
Tetralins of Structure **5**



Entry	R_5	R_7	*Yield* (%)	*m.p.* (°C)
5a	F	F	91	–
5b	CH_3	CH_3	94	–
5c	$CH(CH_3)_2$	$CH(CH_3)_2$	95	–
5d	OCH_3	OCH_3	80	–

TABLE 6
Tetralins of Structure **6**

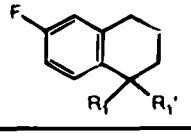


Entry	R_5	R_7	*Yield* (%)	*m.p.* (°C)
6a	F	F	58	—
6b	OCH_3	F	46	—
6c	OCH_3	OCH_3	6	85

by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 14–100%.

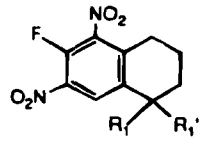
2.2.2. Procedure B: general procedure for the Friedel-Crafts acylation (**1e**, **2c**, **4a–b,d**, **6a,c**)
A solution of the tetrahydronaphthalene (0·010 mol) dissolved in 1,2-dichloroethane (10 ml) was added dropwise to a cold (0°C) solution of anhydrous aluminum

TABLE 7
Tetralins of Structure **7**



Entry	R_1	R'_1	*Yield* (%)	*m.p.* (°C)
7a	CH_3	H	82	—
7b	CH_3	CH_3	88	—
7c	$CH(CH_3)_2$	CH_3	100	—
7d	C_3H_7	C_3H_7	96	—
7e	Spirocyclohexyl		100	—

TABLE 8
Tetralins of Structure **8**

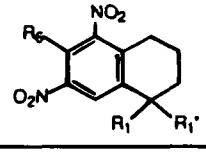


Entry	R_1	R'_1	*Yield* (%)	*m.p.* (°C)
8a	CH_2	H	20	—
8b	CH_3	CH_3	30	92–93
8c	$CH(CH_3)_2$	CH_3	61	80–81
8d	C_3H_7	C_3H_7	67	144–145
8e	Spirocyclohexyl		28	164–165

chloride (0·013 mol) and acid chloride (0·011 mol) in 1,2-dichloroethane (50 ml). The solution was closely monitored during addition to maintain the temperature at 0°C and was stirred for 15 minutes to several hours after complete addition. The solution was poured over ice/water (500 g) and subsequently extracted with diethyl ether. The ether layer was washed with water and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 6–89%.

2.2.3 Procedure C: general procedure for the Haloform reaction with methyl ketones (**1f**, **2d**, **4d**)
At 0°C, 2·5 M sodium hydroxide (52 ml, 0·13 mol) was treated dropwise with bromine (5·3 g, 0·033 mol). The solution was closely monitored during addition to maintain the temperature below 5°C. Upon complete addition, the solution was diluted with cold 1,4-dioxane (30 ml), and this pre-made solution of sodium hypobromite was added dropwise to a solution of the methyl

TABLE 9
Tetralins of Structure **9**



Entry	R_1	R'_1	R_6	*Yield* (%)	*m.p.* (°C)
9a	CH_3	H	$NHCH(C_2H_5)_2$	92	—
9b	$CH(CH_3)_2$	CH_3	$NHCH(C_2H_3)_2$	97	—
9c	$CH(CH_3)_2$	CH_3	$N(CH_3)_2$	100	111–112
9d	$CH(CH_3)_2$	CH_3	OCH_3	100	—
9e	C_3H_7	C_3H_7	$NHCH(C_2H_5)_2$	65	87–88
9f	C_3H_7	C_3H_7	$N(CH_3)_2$	61	—
9g	Spirocyclohexyl		$NHCH(C_2H_5)_2$	86	94–95
9h	Spirocyclohexyl		$N(CH_3)_2$	87	95–96

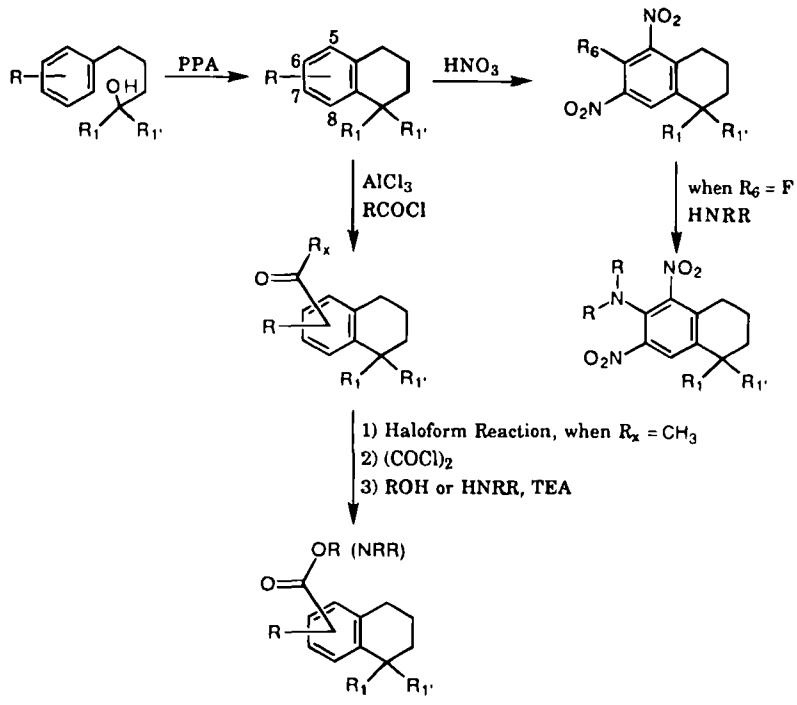


Fig. 2. Generalized synthesis of tetrahydronaphthalenes.

ketone (0·010 mol) and water (30 ml) in 1,4-dioxane (100 ml) at 0°C. Upon complete addition, the solution was stirred at room temperature for 1–14 h. Anhydrous sodium sulfite (3.0 g) in water (15 ml) was added to destroy the remaining sodium hypobromide. The solution was poured over ice/hydrochloric acid (200 g) and subsequently extracted with diethyl ether. The ether layer was washed with water and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 89–100%.

2.2.4 Procedure D: general procedure for the preparation of carboxylate esters and amides (**1g, 2e, 4e–h**)

Oxalyl chloride (0·050 mol) and one drop of *N,N'*-dimethylformamide were added to the acid (0·010 mol) dissolved in dichloromethane (50 ml). After the solution had been stirred at room temperature for 15 minutes to several hours, the solvent was removed to give the acid chloride. The acid chloride (0·010 mol) was dissolved in dichloromethane (20 ml) and this was added to a solution of the alcohol or amine (0·011 mol) and triethylamine (2 ml) in dichloromethane (20 ml). After the solution had been stirred at room temperature for 15 minutes to several hours, the solvent was removed and the residue was mixed with diethyl ether and water. The mixture was washed with water, 3% aqueous hydrochloric acid, water, saturated sodium hydrogen carbonate, water, and brine. The solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the product. The product was purified by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 72–93%.

2.2.5 Procedure E: general procedure for nitration using fuming nitric acid (**1d, 2b, 8a–e, 10**)

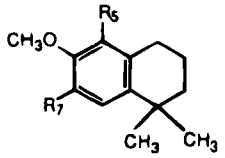
The tetralin (0·010 mol) was added in small portions over a period of 15–60 min to fuming nitric acid (20 ml) chilled to −5°C (methanol/ice). The solution was closely monitored to keep the temperature below 7°C. Upon complete addition, the solution was stirred at room temperature for up to 7 h, poured over ice/water (500 g), and subsequently extracted with methylene chloride. The methylene chloride layer was washed with water and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. (If reaction would not go to completion, the same procedure was repeated on the mixture.) The product was purified by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 20–67%.

2,3-dihydro-1,1,5-trimethyl-4,6-dinitro-1*H*-indene (**10**). A yellow solid (29%), m.p. 81–82°C; [^{1}H] NMR (deuterochloroform) ppm; 1·30(s,6H), 2·04(t,2H), 2·43(s, 3H), 3·00(t,2H), 7·73(s,1H); Calcd for $C_{12}H_{14}N_2O_4$: C, 57·59; H, 5·64. Found: C, 57·52; H, 5·63.

2.2.6 Procedure F: general procedure for the reaction of 6-fluoro tetralins with amines (**3a–f, 9a–c, e–h**)

Excess amine was added to 6-fluorotetralin (0·010 mol) dissolved in dichloromethane (30 ml). After the solution

TABLE 10
Soil-Applied Herbicidal Activity of Compounds of General Structure **1**



			Primary (Avg %) (% phytotoxicity)		*Secondary (Avg GR_{80}) (Kg ha^{-1})*			
					Warm Season		*Cool Season*	
Entry	R_5	R_7	*MC*[a]	*DC*[a]	*MC*	*DC*	*MC*	*DC*[b]
1a	H	H	0	0	—	—	—	—
1b	NO_2	H	50	8	6·9	9·6	8·5	8·1
1c	H	NO_2	38	4	1·1	>11·2	11·2	>11·2
1d	NO_2	NO_2	40	0	2·7	>11·2	4·4	5·3
1e	H	$COCH_3$	58	8	4·8	>11·2	11·2	>11·2
1f	H	CO_2H	0	0	—	—	—	—
1g	H	CO_2CH_3	0	0	—	—	—	—

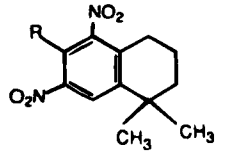
[a] Average of monocotyledonous (MC) or dicotyledonous (DC) weeds, only.
[b] Average of dicotyledonous weeds plus oilseed rape.

had been stirred for 1–14 hs, the solution was washed with water, sodium hydrogen carbonate, and brine. The solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane) or crystallization. Yields were 61–100%.

2.2.7 Preparation of 1,2,3,4-tetrahydro-6-methoxy-1,1-dimethyl-5-nitronaphthalene and 1,2,3,4-tetrahydro-6-methoxy-1,1-dimethyl-7-nitronaphthalene (**1b–c**)

At −0°C, **1a** (1,2,3,4-tetrahydro-6-methoxy-1,1-dimethylnaphthalene) (0·5 g, 0·0026 mol) dissolved in glacial acetic acid (10·0 ml) and acetic anhydride (1 ml), was treated with 70% nitric acid (0·50 g, 0·0055 mol) in

TABLE 11
Soil-Applied Herbicidal Activity of Compounds of General Structure **3**



		Primary (Avg %) (% phytotoxicity)		*Secondary (Avg GR_{80}) (Kg ha^{-1})*			
				Warm Season		*Cool Season*	
Entry	*R*	*MC*	*DC*	*MC*	*DC*	*MC*	*DC*
3a	$NHCH_3$	44	8	4·9	>11·2	10·6	>11·2
3b	$N(CH_3)_2$	30	8	0·95	>11·2	>11·2	>11·2
3c	NHC_2H_5	28	16	0·97	>11·2	5·3	10·8
3d	$N(C_2H_5)_2$	78	24	0·66	>11·2	1·2	>11·2
3e	$N(C_3H_3)_2$	40	0	4·7	>11·2	4·8	>11·2
3f	$NHCH(C_2H_5)_2$	74	54	0·47	>11·2	3·2	2·9
Pendimethalin	—	—	—	0·05	1·2	0·31	0·52
3g	SC_2H_5	58	4	1·1	>11·2	3·0	10·2
3h	$SO_2C_2H_5$	44	0	0·91	>11·2	>11·2	>11·2

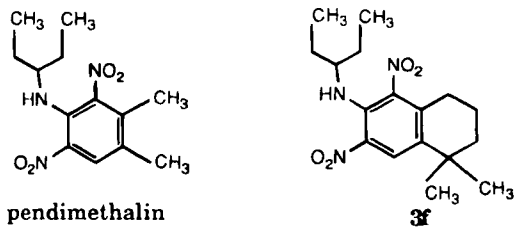


Fig. 3. Structure of **3f** and pendimethalin.

glacial acetic acid (10·0 ml) and acetic anhydride (1·0 ml). The solution was maintained at 0°C and stirred for 2 h at room temperature after complete addition. The solution was poured over ice/water (200 g) and extracted with methylene chloride. The methylene chloride layer was washed with water, sodium hydrogen carbonate, and brine. The solution was dried over magnesium sulfate, filtered, and the solvent was removed to give a mixture of two products. Fraction one of column chromatography (ethyl acetate + hexane; 3 + 97 by volume) gave 0·31 g (50%) of a yellow oil, **1b**; [^{1}H] NMR (deuterochloroform) ppm: 1·18(s,6H), 1·56(m,2H), 1·70(m,2H), 2·56(t,2H), 3·77(s,3H), 6·77(d,1H,J = 8·8 Hz), 7·30(d,1H,J = 8·8 Hz); Calcd for $C_{13}H_{17}NO_3$: C, 66·36; H, 7·28. Found: C, 66·63; H, 7·31. Fraction two of column chromatography (ethyl acetate + hexane; 3 + 97 by volume) gave 0·31 g (50%) of a white solid, **1c**, m.p. 130–131°C; [^{1}H] NMR (deuterochloroform) ppm: 1·20(s,6H), 1·60(m,2H), 1·73(m,2H), 2·72(t,2H), 3·84(s,3H), 6·64(s,1H), 7·79(s,1H); Calcd for $C_{13}H_{17}NO_3$: C, 66·36; H, 7·28. Found: C, 66·41; H, 7·32.

2.2.8 Preparation of 6-*(ethylthio)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene* (**3g**)

A 90% ethanethiol sodium salt (0·34 g, 0·0036 mol) was added to **8b** (6-fluoro-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene) (0·82 g, 0·0031 mol) dissolved in methanol (20 ml). After stirring for 1 h, the solution was washed with water, sodium hydrogen carbonate, and brine. The solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane; 5 + 95 by volume) to give 0·85 g (90%) of a yellow solid, **3g**, m.p. 97–98°C; [^{1}H] NMR (deuterochloroform) ppm: 1·19(t,3H), 1·32(s, 6H), 1·69(m,2H), 1·83(m,2H), 2·65(t,2H), 2·93(q,2H), 7·76(s,1H); Calcd for $C_{14}H_{18}SN_2O_4$: C, 54·18; H, 5·85. Found: C, 54·23; H, 5·84.

2.2.9 Preparation of 6-(ethylsulfonyl)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitro-naphthalene (**3h**)

A solution of 50% *m*-chloroperoxybenzoic acid (1·06 g, 0.0033 mol) in dichloromethane (30 ml) was added slowly to a solution of **3g** (6-(ethylthio)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene) (0·50 g, 0·0016 mol) in dichloromethane (25 ml) at 0°C. The solution was stirred at room temperature for 2 h and subsequently washed with water, sodium hydrogen carbonate, and brine. The solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by recrystallization from hexane to give 0·51 g (76%) of a yellow solid, **3h**, m.p. 152·5–153·5°C; [^{1}H] NMR (deuterochloroform) ppm: 1·35(s,6H), 1·50(t,3H), 1·55(m, 2H), 1·73(m,2H), 2·68(t,2H), 3·65(q,2H), 7·24(s,1H), 8·26(s,1H); Calcd for $C_{14}H_{18}SN_2O_6$: C, 64.42; H, 8·50. Found: C, 64·44; H, 8·53.

2.2.10 Preparation of 1-(3-fluoro-5,6,7,8-tetrahydro-1-methoxy-5,5-dimethyl-2-naphthalenyl)-ethanone (**6b**)

Sodium methoxide, 95% (0·40 g, 0·0070 mol) was added to a solution of **6a** [1-(1,3-difluoro-5,6,7,8-tetrahydro-5,5-dimethyl-2-naphthalenyl)ethanone] (0·75 g, 0·0031 mol) in methanol (20 ml). The solution was stirred at reflux overnight, poured into water (50 ml), and extracted with diethyl ether. The ether layer was washed with water and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane 5 + 95 by volume) to give 0·36 g (46%) of a yellow oil, **6b**; [^{1}H] NMR (deuterochloroform) ppm: 1·18(s,6H), 1·56(m,2H), 1·70(m,2H), 2·48(d,3H, J_{HF} = 1·6 Hz), 2·60(t,2H), 3·66(s, 3H), 6·78(dt,1H, J_{HF} = 11·4 Hz). [^{19}F] NMR (deuterochloroform) ppm: −120·64(s); Calcd for $C_{15}H_{19}FO_2$: C, 71·98; H, 7·65. Found: C, 71·96; H, 7·60.

2.2.11 Preparation of 1,2,3,4-tetrahydro-6-methoxy-1-methyl-1-(1-methylethyl)-5,7-dinitronaphthalene (**9d**).

Sodium methoxide, 95% (0·10 g, 0·017 mol) was added to a solution of **8c** (6-fluoro-1,2,3,4-tetrahydro-1-methyl-1-(1-methylethyl)-5,7-dinitronaphthalene (0·40 g, 0·0013 mol) in methanol (20 ml). The solution was stirred at 55°C for 1 h, poured into water (200 ml), and extracted with diethyl ether. The ether layer was washed with water, sodium hydrogen carbonate and brine, and the solution was dried over magnesium sulfate, filtered, and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate + hexane; 3 + 97 by volume) to give 0·40 g (100%) of a yellow oil, **9d**; [^{1}H] NMR (deuterochloroform) ppm: 0·60(d,3H), 0·93(d,3H), 1·22(s, 3H), 1·50(m,1H), 1·65(m,2H), 1·88(m,1H), 2·06(septet, 1H), 2·55(m,2H), 3·90(s,3H), 7·92(s,1H); Calcd for $C_{16}H_{20}N_2O_5$: C, 58·43; H, 6·54. Found: C, 58·57; H, 6·56.

2.3 Determination of herbicidal activity

2.3.1 Primary pre-emergence herbicidal screen

A Dupo silt loam soil containing less than 2% organic matter was placed in an aluminum pan and compacted

with furrows to a depth of approximately 1·27 cm from the top of the pan. Seeds of yellow nutsedge, annual bluegrass, seedling johnsongrass, downy brome, barnyardgrass, annual morningglory, cocklebur, velvetleaf, Indian mustard, and wild buckwheat were placed in the furrows prior to chemical treatment. A known amount of the test compound was dissolved in acetone to give a 10 g litre^{-1} solution, and a dilution was made from this stock solution to provide a rate of 11·2 kg ha^{-1}. The chemical solution was subsequently sprayed over the entire pan with the seeds exposed in the furrows. The seeds were subsequently covered with a layer of soil to completely fill the pan, and the pans were placed in a greenhouse maintained at day/night temperatures of 30/21°C. All pans were watered by subirrigation, and the species were rated visually against an untreated control at approximately 14 days after application. The rating scale ranged from 0 to 100 with 0 representing no injury and 100 complete death of the plant, and the data are presented as averages over the monocotyledons of annual bluegrass (*Poa annua* L.), seedling johnsongrass (*Sorghum halepense* (L.) Pers.), downy brome (*Bromus tectorum* L.), and barnyardgrass (*Echinochloa crus-galli* (L.) Beauv.) and dicotyledons annual morningglory (*Ipomea spp.*), cocklebur (*Xanthium stumarium* L.), velvetleaf (*Abutilon theophrasti* Medic.), Indian mustard (*Brassica juncea* (L.) Coss.), and wild buckwheat (*Polygonum convolvulus* L.). The monocotyledon average also includes the yellow nutsedge (*Cyperus esculentus* L.) component. Compounds with sufficient herbicidal activity were selected for evaluation in the secondary screen while all others were eliminated from further testing.

2.3.2 Secondary pre-plant incorporated herbicidal screen

All pans used for the herbicide screen were prepared as described above. In one pan, seeds of corn (*Zea mays* L.), rice (*Oryza sativa* L.), soybean (*Glycine max* (L.) Merr.), cotton (*Gossypium hirsutum* L.), large crabgrass (*Digitaria sanguinalis* (L.) Scop.), seedling johnsongrass, barnyardgrass, velvetleaf, annual morningglory, and cocklebur, which comprise the warm-season spectrum, were placed in the furrows. In a second pan, the cool-

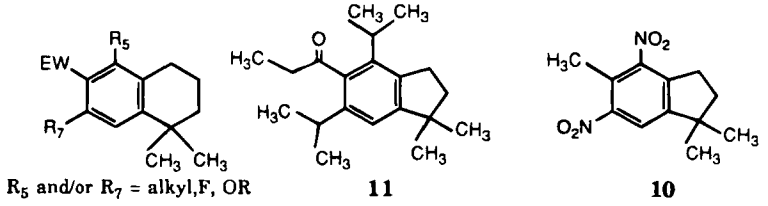
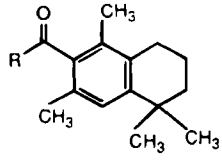


Fig. 4. Structure of indane (**11**) and structurally similar analogs.

TABLE 12
Soil-Applied Herbicidal Activity of Compounds of General Structure **4**



		Primary (Avg %) (% phytotoxicity)		*Secondary (Avg GR_{80}) Warm (Kg ha^{-1}) Cool*			
				Season		*Season*	
Entry	*R*	*MC*	*DC*	*MC*	*DC*	*MC*	*DC*
4a	CH_3	74	34	4·7	11·2	5·0	6·8
4b	C_2H_5	78	54	3·1	>11·2	5·2	7·4
4c	CBr_3	2	4	—	—	—	—
4d	OH	0	0	—	—	—	—
4e	OCH_3	94	72	0·59	6·7	0·85	3·4
4f	OC_2H_5	76	36	4·5	>11·2	7·8	9·4
4g	OC_4H_9	2	2	—	—	—	—
4h	$N(CH_3)_2$	4	4	>11·2	>11·2	>11·2	>11·2
11	–	80	52	0·4	9·6	0·16	1·0
10	–	84	54	1·1	8·1	1·6	5·4

season spectrum consisting of wheat (*Triticum aestivum* L.), oilseed rape (*Brassica napus* L.), wild oat (*Avena futua* L.), downy brome, blackgrass (*Alopecurus myosuroides* Huds.), green foxtail (*Setaria viridis* (L.) P. Beauv.), cleavers (*Galium aparine* L.), wild buckwheat, common chickweed (*Stellaria media* (L.) Vill.), and Russian thistle (*Salsola kali* L.) were seeded in the furrows. From the 10 g litre^{-1} stock solution prepared above, aliquots were taken to make dilutions which corresponded to rates ranging from 0·07 to 11·2 kg ha^{-1}. All chemical treatments were made by mixing the appropriate solution with the layer of soil needed to cover the seeds in the pans. The pans containing the warm-season species were placed in a greenhouse maintained at day/night temperatures of 30/21°C, and the pans containing the cool-season species were maintained at day/night temperatures of 24/16°C. The pans were initially overhead irrigated with approximately 0·5 cm of water and all subsequent moisture was supplied through subirrigation. At approximately 14 days after treatment, all species were rated visually as described above. All data for the weeds from the secondary screen were converted to average GR_{80} values which is the amount of herbicide, in kg ha^{-1}, that caused an average of 80% injury over a given subset of weeds. This GR_{80} value was determined by extrapolation between two adjacent rates in the titration where the higher rate had an average of greater than 80% injury and the lower rate had an average of less than 80% injury. If the average of 80% injury occurred at the actual applied rate, then that value was selected for the GR_{80}. The variability of the data in these tests has been determined to be a factor of ± 2 in the rate titration.

3 RESULTS AND DISCUSSION

The tetralins described can be divided into two classes: (1) those that 'structurally' mimic the dinitroaniline class of chemistry and (2) those that 'structurally' mimic the indane classes of chemistry. All tetralins and indanes[4] with herbicide activity caused symptoms of mitotic inhibition, which included severe root pruning, stunting, and lack of emergence. These symptoms were similar to those produced by the dinitroanilines[5] which suggests that these compounds may be inhibitors of tubulin formation.[6]

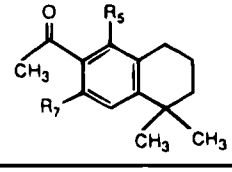
Table 10 shows the herbicidal activity for the 6-methoxytetralin analogs (**1a–g**). These compounds exhibited similar activity trends to the 6-alkyltetralin analogs in that electron-withdrawing groups (NO_2, $COCH_3$) at the 5- and/or 7-position may be necessary for herbicidal activity.[3] However, these compounds were less active than the corresponding 6-methyltetralin analogs. The 8-methoxytetralin analogs (**2a–e**) (Table 2) had very little activity.

Table 11 shows the herbicidal activity for the 6-amino and 6-thiotetralin analogs (**3a–h**). As a group the 6-aminotetralins proved to be the most active, with **3f** possessing the highest unit activity. This series of tetralins are the most similar in structure to the dinitroanaline class. In particular, the structures of **3f** and the dinitroanaline pendimethalin, *N*-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine, ('Prowl'®; American Cyanamid) differ only in the fused cyclohexane ring substitution versus the dimethyl substitution (Fig. 3). However, **3f** was substantially less active than pendimethalin.

The herbicidal activities of the 6-thiotetralin analogs **3g,h** were comparable in unit activity to those of the 6-alkyltetralin analogs.[3]

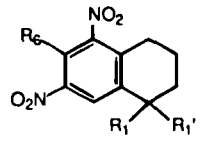
Another series of tetralins were prepared that structurally mimicked the indanes which included **11**. In terms of structural comparison to the tetralins, the indanes have a fused 5,6 ring system rather than the fused 6,6 system of the tetralins. Two sets of tetralin analogs were targeted based on structural similarity to

TABLE 13
Soil-Applied Herbicidal Activity of Compounds of General Structure **6**



			Primary (Avg %) (% phytotoxicity)		*Secondary (Avg GR_{80}) Warm (Kg ha^{-1}) Cool*			
					Season		*Season*	
Entry	R_5	R_7	*MC*	*DC*	*MC*	*DC*	*MC*	*DC*
6a	F	F	14	8	>11·2	>11·2	>11·2	>11·2
6b	OCH_3	F	68	24	—	—	—	—
6c	OCH_3	OCH_3	—	—	1·0	4·8	2·7	5·0

TABLE 14
Soil-Applied Herbicidal Activity of Compounds of General Structure **9**



				Primary (Avg %) (% phytotoxicity)	
Entry	R_1	R_1'	R_6	*MC*	*DC*
9a	CH_3	H	$NHCH(C_2H_3)_2$	24	0
9b	$CH(CH_3)_2$	CH_3	$NHCH(C_2H_3)_2$	24	0
9c	$CH(CH_3)_2$	CH_3	$N(CH_3)_2$	34	2
9d	$CH(CH_3)_2$	CH_3	OCH_3	32	6
9e	C_3H_7	C_3H_3	$NHCH(C_2H_3)_2$	0	0
9f	C_3H_7	C_3H_3	$N(CH_3)_2$	16	2
9g	Cyclohex		$NHCH(C_2H_3)_2$	4	2
9h	Cyclohex		$N(CH_3)_2$	28	0

indane **11**. The first series of compounds maintains the substitution pattern of the aromatic ring of the indanes in which R_6 = an electron-withdrawing group (EN) while $R_5 = R_7$ = alkyl, fluorine, or alkoxy and changes the 5-membered non-aromatic ring to a 6-membered non-aromatic ring. The second target included a single compound (**10**) that maintains the 5-membered non-aromatic ring of the indanes and changes the substitution pattern of the aromatic ring to the 5,7-dinitro-6-methyl which exhibited the greatest overall activity of the 6-methyltetralin analogs (Fig. 4).

Table 12 shows the herbicidal activity for the 6-keto-5,7-dimethyltetralin analogs, indane **11**, and the target compound **10**. A relatively high degree of unit activity was obtained by altering the substitution pattern on the aromatic ring as compared to the previous tetralins. As the esters increase in size and herbicidal activity decreases with the methyl ester (**4e**) being the most active of the tetralins. However, indane **11** was the most active, and considerably more active than the direct analog **4b**. Compound **10** was similar in activity to its direct tetralin analog (fused 6,6-ring system.)[3]

The compounds (**5a–d**) in Table 5 which were intermediates showed a general lack of herbicidal activity. The only compound to demonstrate any control was **5d** with the dimethoxy substituents. In the series of tetralins (**6a–c**) in Table 13, replacing the methoxy groups with fluoro substituents greatly decreased activity.

Thus far, emphasis has been placed primarily on variations of the aromatic ring substituents. Table 14 contains a series of tetralin analogs in which the dimethyl groups at the 1-position have been substituted with various alkyl groups in an effort to increase herbicidal activity. However, the dimethyl substituents at the 1-position (R_1, R_1') were the most active as any other combination of alkyl substituents greatly reduced herbicide activity (Table 14). Substituting a fluorine at the 6-position tended to inactivate the tetralins, regardless of substitution at R_1 and R_1' (Tables 7 & 8).

In summary, the greatest herbicidal activities were obtained when R_5 and R_7 = nitro or methyl, R_6 = ester or amino, R_8 was unsubstituted, and R_1, R_1' = methyl. Substitution of the phenyl ring with a fluorine at R_5, R_6, or R_7 or replacement of hydrogen at the R_8 position tended to inactivate the molecule. Also, substituting the non-aromatic ring with substituents other than methyl at R_1, R_1' greatly reduced activity. The best overall herbicide activity was obtained with compound **4e** when R_5, $R_7 = CH_3$, $R_6 = -C(O)OCH_3$, $R_8 = H$, and $R_1, R_1' = -CH_3$.

A steric and electronic model is proposed for the tetrahydronaphthalenes and will be described in a future publication.

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